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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/674,065	09/30/2003	A. Robin Poole	079328-0105	1202

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EXAMINER	
ROBINSON, HOPE A	
ART UNIT	**PAPER NUMBER**
1656	

DATE MAILED: 12/08/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/674,065	POOLE, A. ROBIN	
	Examiner	Art Unit	
	Hope A. Robinson	1656	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *22 September 2005*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-92* is/are pending in the application.

4a) Of the above claim(s) *6-67 and 74-92* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-5 and 68-73* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☒ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *30 September 2003* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☒ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date *4/30/04*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

Application Status

1. Applicant's election with traverse of Group I (claims 1-73, SEQ ID NO:3), on September 22, 2005 is acknowledged. The traversal is on the grounds that the claims not be restricted as there is no burden of search. Applicant points to MPEP 803 for support. This argument is not persuasive as the claims are directed to several different amino acid sequences, which presents a search burden. Furthermore, the application has several other inventions such as antibodies and methods as set forth in the Restriction Requirement. The search burden is also demonstrated by the separate status that each invention has acquired in the art, which indicates that the search is not coextensive. However, if applicant is willing to make a statement on the record that a reference that anticipates or renders obvious one protein would also anticipate or render obvious other proteins in the application then they will be rejoined. In addition MPEP chapter 800 state that restriction is proper if the claimed invention could be shown to be independent and or distinct (see MPEP 806). The restriction requirement of record has established that the application has several patentably distinct inventions for the reasons of record and as applicant's statements are not persuasive, the restriction requirement is proper and final.

Claim Disposition

2. Claims 1, 6, 11, 16, 21, 26, 32, 35, 43, 48, 53, 58 and 63 are amended. Claims 1-92 are pending. Claims 1-5 and 68-73 are under examination. Claims 6-67 and 74-92 are withdrawn from further consideration pursuant to 37 CFR 1.12(b), as being drawn to a non-elected invention, there being no allowable generic or linking claim. Note that claim 6-67 are withdrawn from consideration, as applicant elected SEQ ID NO:3, the claims are directed to a non-elected invention. Further, claims 1 and 68-73 are only being examined to the extent that the claims pertain to the elected invention. Applicant is advised to cancel the non-elected subject matter in the claims.

3. The Amendment filed on February 27, 2004 has been received and entered.

Specification

4. The specification is objected to because of the following informalities:

The specification is objected to because trademarks are disclosed throughout the instant specification and not all of them are capitalized or accompanied by the generic terminology. The use of the trademarks such as TRITON-X-100®, TWEEN-20®, for example, have been noted in this application (see pages 40-41). It should be capitalized wherever it appears and be accompanied by the generic terminology. Although the use of trademarks is permissible in patent applications, the proprietary nature of the marks should be respected and every effort made to prevent their use in any manner, which might adversely affect their validity as trademarks.

Correction of the above is required.

Drawing

5. The Drawing filed on September 30, 2003 has been accepted by the examiner.

Sequence Compliance

6. This application contains sequence disclosures that are encompassed by the definitions for nucleotide and/or amino acid sequences set forth in 37 CFR 1.821(a)(1) and (a)(2). However, this application fails to comply with the requirements of 37 CFR1.821 through 1.825; applicant's attention is directed to the final rule making notice published at 55 FR 18230 (May 1, 1990), and 1114 OG 29 (May 15, 1990). To be in compliance, applicant is required to identify all amino acid sequences of at least 4 L-amino acids and at least 10 nucleotides by a sequence identifier, i.e., "SEQ ID NO:". The specification discloses sequences that have not been identified by a sequence identifier, see for example, page 9 and throughout the instant specification. In addition, the Figures disclose sequences, however the Brief Description of the Drawings does not describe the sequence identifiers (see Fig 1. If these sequences have not been disclosed in the computer readable form of the sequence listing and the paper copy thereof, applicant must provide a computer readable form of the "Sequence Listing" including these sequences, a paper copy of the "Sequence Listing", as well as an amendment directing its entry into the specification, and a statement that the content of the paper and computer readable form copies are the same and, where applicable,

include no new matter as required by 37 CFR 1.821(e) or 1.821(f) or 1.821(g) or 1.821(b) or 1.825(d). See the attached Notice to Comply with the sequence rules.

Oath/Declaration

7. The Oath/Declaration is objected to because of the following informalities:

The oath/declaration is objected to because non-initialed and/or non-dated alterations have been made to the oath or declaration (see inventor Robin Poole). See 37 CFR 1.52(c).

Correction is required.

Claim Objection

8. Claims 68-69 are objected to because of the following informalities:

Claims 68 and 69 are objected to for the recitation of "A peptide as in any one of claim..." instead of "The peptide as in any one of claim...".

Claim 69 is objected to because the claim recites 'homology' which pertains to ancestral links, it is suggested that the claim is amended to recite "sequence identity" as the claim is comparing the sequence alignment of a sequence of interest to another sequence.

Correction of the above is required.

Information Disclosure Statement

9. The Information Disclosure Statement filed on April 30, 2004 has been received and entered. The references cited on the PTO-1449 Form have been considered by the examiner and a copy is attached to the instant Office action.

Claim Rejections - 35 USC ∋ 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

10. Claims 1-5 and 68-73 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

The claimed invention is directed to an isolated or purified peptide (SEQ ID NO:3) and a fragment thereof. The claims are also directed to a peptide that has at least 80% homology to the peptide as claimed. The claims also encompass peptide dimers and trimers. A skilled artisan cannot envision the detailed chemical structure for said dimer, trimer or all the fragments encompassed in the claim. The claims encompass a genus of fragments that are highly variable.

The specification fails to provide any additional representative species of the claimed genus to show that applicant was in possession of the claimed genus. A representative number of species means that the species, which are adequately described are representative of the entire genus. The written description requirement for a claimed genus may be satisfied through sufficient description of a representative number of species by actual reduction to practice, disclosure of drawings, or by disclosure of relevant identifying characteristics, for example, structure or other physical and/or chemical properties, by functional characteristics coupled with a known or disclosed correlation between function and structure, or by a combination of such identifying characteristics, sufficient to show the applicant was in possession of the claimed genus.

Accordingly, in the absence of sufficient recitation of distinguishing identifying characteristics, the specification does not provide adequate written description of the claimed genus. The claimed genus of peptides could include non-functional proteins or proteins with a different function than the one described. Therefore, the genus of claimed peptides encompasses widely variant species. As such, neither the description of the structure and function of SEQ ID NOS: 3, for example, "80% sequence identity to SEQ ID NO:3 and is effective in altering the rate of degradation of type II collagen or the rate of chrondrocyte hypertrophy is sufficient to be representative of the attributes and features of the entire genus.

Vas-Cath Inc. v. Mahurkar, 935 F.2d 1555, 1563-64, 19 USPQ2d 1111, 1117 (Fed. Cir.1991), states that "applicant must convey with reasonable clarity to those skilled in the art that, as of the filing date sought, he or she was in *possession of the*

invention. The invention is, for purposes of the 'written description' inquiry, *whatever is now claimed*" (See page 1117). The specification does not "clearly allow persons of ordinary skill in the art to recognize that [he or she] invented what is claimed" (See *Vas-Cath* at page 1116). The skilled artisan cannot envision the detailed chemical structure of the encompassed genus of polypeptides, and therefore, conception is not achieved until reduction to practice has occurred, regardless of the complexity or simplicity of the method of isolation. Adequate written description requires more than a mere statement that it is part of the invention and reference to a potential method of isolating it. The compound itself is required. *See Fiers v. Revel, 25 USPQ2d 1601 at 1606 (CAFC 1993).*

Therefore, for all these reasons the specification lacks adequate written description, and one of skill in the art cannot reasonably conclude that the applicant had possession of the claimed invention at the time the instant application was filed.

11. Claims 1-5 and 68-73 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for the proteins set forth in SEQ ID NO: 3, does not reasonably provide enablement for any peptide fragment thereof or peptides or having at least 80% sequence homology to SEQ ID NO: 3. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make the invention commensurate in scope with these claims. The enablement requirement refers to the requirement that the specification describe how to

make and how to use the invention. There are many factors to be considered when determining whether there is sufficient evidence to support a determination that a disclosure does not satisfy the enablement requirement and whether any necessary experimentation is undue. These factors include, but are not limited to: Quantity of Experimentation Necessary; Amount of direction or guidance presented; Presence or absence of working examples; Nature of the Invention; State of the prior art and Relative skill of those in the art; Predictability or unpredictability of the art and Breadth of the claims (see *In re Wands, 858 F.2d at 737, 8 USPQ2d at1404 (Fed. Cir. 1988*). The factors most relevant to the instant invention are discussed below.

The amount of experimentation required to practice the claimed invention is undue as the claims encompass an unspecified amount of peptide fragments of the sequences set forth in SEQ ID NO: 3. No correlation is made between structure and function of the claimed peptides. In addition, the claims are directed to "1-5 conservative amino acid substitutions" or "a conservatively substituted variant thereof" or "fragments thereof" and there is no indication in the claims where in the sequence changes will occur to construct said fragment/variant or whether function will be retained, or be different or is nonfunctional. In addition, claims reciting percent sequence identity, for example 80% sequence identity (claim 69) do not indicate where variations will occur or what variations can be tolerated in the sequence. The instant specification does not demonstrate or provide guidance as to what the structure of the protein will be once modified or if said protein will be functional or exhibit the same properties or characteristics as the native protein. In the instant application, the partial structure in

the form of the recited percent identity is insufficient to determine a chemical structure for the variants encompassed in the claims. Additionally, there is no data provided demonstrative of a particular portion of the structure that must be conserved. Therefore, the claims encompass variants/fragments that may not have any biological activity. Due to the large quantity of experimentation necessary to generate the infinite number of variants/fragments recited in the claims and possibly screen same for activity and the lack of guidance/direction provided in the instant specification, this is merely an invitation to the skilled artisan to use the current invention as a starting point for further experimentation. Thus, undue experimentation would be required for a skilled artisan to make and/or use the claimed invention commensurate in scope with the claims.

Predictability of which potential changes can be tolerated in a protein's amino acid sequence and obtain the desired activity requires a knowledge of and guidance with regard to which amino acids in the protein's sequence, if any, are tolerant of modification and which are conserved (for example, expectedly intolerant to modification), and detailed knowledge of the ways in which the protein's structure relates to its function. In addition, one skilled in the art would expect any tolerance to modification for a given protein to diminish with each further and additional modification, for example, multiple substitutions. In this case, the necessary guidance has not been provided in the specification. Therefore, while it is known in the art that many amino acid substitutions are possible in any given protein, the positions within the protein's sequence where such amino acid substitutions can be made with a reasonable expectation of success are limited, as certain positions in the sequence are critical to

the protein's structure/function relationship. It is also known in the art that a single nucleotide or amino acid change or mutation can destroy the function of the biomolecule in many cases. For example, various sites or regions directly involved in binding activity and in providing the correct three-dimensional spatial orientation of binding and active sites can be affected (see Wells, Biochemistry, vol. 29, pages 8509-8517, 1990). The instant specification provides no guidance/direction as to which regions of the protein would be tolerant of modifications and which would not, and it provides no working examples of any variant sequence that is encompassed by the claims. It is in no way predictable that randomly selected mutations, such as deletions, substitutions, additions, etc., in the disclosed sequences would result in a protein having activity comparable to the one disclosed. As plural substitutions for example are introduced, their interactions with each other and their effects on the structure and function of the protein is unpredictable. The skilled artisan would recognize the high degree of unpredictability that all the fragments/variants encompassed in the claims would retain the recited function.

The state of the prior art provides evidence for the high degree of unpredictability as stated above. Seffernick et al. (J. Bacteriology, vol. 183, pages 2405-2410, 2001) disclose two polypeptides having 98% sequence identity and 99% sequence identity, differing at only 9 out of 475 amino acids (page 2407, right column, middle and page 2408, Fig. 3). The polypeptides of Seffernick et al. are identical along relatively long stretches of their respective sequences (page 2408, Fig. 3), however, these polypeptides exhibit distinct functions. The modifications exemplified in the Seffernick

et al. reference is small compared to those contemplated and encompassed by the claimed invention.

The specification lacks adequate guidance/direction to enable a skilled artisan to practice the claimed invention commensurate in scope with the claims. Furthermore, while recombinant and mutagenesis techniques are known in the art, it is not routine in the art to screen large numbers of mutated proteins where the expectation of obtaining similar activity is unpredictable based on the instant disclosure. The amino acid sequence of a protein determines its structural and functional properties, and predictability of what mutations can be tolerated in a protein's sequence and result in certain activity, which is very complex, and well outside the realm of routine experimentation, because accurate predictions of a protein's function from mere sequence data are limited, therefore, the general knowledge and skill in the art is not sufficient, thus the specification needs to provide an enabling disclosure.

The working examples provided do not rectify the missing information in the instant specification pertaining to the claimed variant. The nature and properties of this claim is difficult to ascertain from the examples provided as one of skill in the art would have to engage in undue experimentation to construct the variants of the claimed invention and examine the same for function.

The specification does not provide support for the broad scope of the claims, which encompass an unspecified amount of variants/fragments of the peptides. The claims broadly read on any fragment thereof for the given sequence (SEQ ID NO: 3). The issue in this case is the breath of the claims in light of the predictability of the art as

determined by the number of working examples, the skill level artisan and the guidance presented in the instant specification and the prior art of record. This make and test position is inconsistent with the decisions of *In re Fisher, 427 F.2d 833, 839, 166 USPQ 18, 24 (CCPA 1970)* where it is stated that "...scope of claims must bear a reasonable correlation to scope of enablement provided by the specification to persons of ordinary skill in the art...". Without sufficient guidance, determination of having the desired biological characteristics is unpredictable and the experimentation left to those skilled in the art is unnecessarily and improperly extensive and undue. See *In re Wands, 858 F.2d at 737, 8 USPQ2d at 1404 (Fed. Cir. 1988)*. Therefore, absent direction/guidance regarding whether the structure of the peptide can tolerate the modifications contemplated a non-functional protein may result and one of skill in the art would not be able to practice the claimed invention commensurate in scope with the claims. In addition, absent direction/guidance regarding the trimer/dimer peptides one of skill in the art would not be able to make the claimed peptide.

Thus, for all these reasons, the specification is not considered to be enabling for one skilled in the art to make and use the claimed invention as the amount of experimentation required is undue, due to the broad scope of the claims, the lack of guidance and working examples provided in the specification and the high degree of unpredictability as evidenced by the state of the prior art, attempting to construct and test variants of the claimed invention would constitute undue experimentation. Making and testing the infinite number of possible variants to find one that functions as described is undue experimentation. Therefore, applicants have not provided sufficient

guidance to enable one of skill in the art to make and use the claimed invention in a manner that reasonably correlates with the scope of the claims, to be considered enabling.

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter, which the applicant regards as his invention.

12. Claims 1-5 and 68-73 are rejected under 35 U.S.C. 112, second paragraph, as failing to set forth the subject matter, which applicant (s) regard as their invention.

(a) Claim 1 is indefinite for the recitation of "altering the rate of degradation" as it is unclear how the rate is altered, is this, an increase or decrease? Claim 1 is also indefinite as the claim has an improper Markush listing, the proper grouping should be "A, B and C" or "A, B or C". Presently the claim language is "A or B or C". The dependent claims hereto are also included in this rejection.

(b) Claims 2-5 lack antecedent basis for the recitation of "the peptide fragment of claim 1" as independent claim 1 is directed to "an isolated or purified peptide".

(c) Claim 68 is indefinite for the recitation of "1-5 acids of the peptide", as the metes and bounds of the claim is unclear. The claim should be amended to recite "amino acids".

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

13. Claims 1 and 69 are rejected under 35 U.S.C. 102(b) as being anticipated by Qvist et al. (U.S. Patent No. 6,110,689, August 29, 2000).

Qvist et al. teach a sequence that is 100% identical to the peptide sequence set forth in SEQ ID NO: 3 of the instant application (see the alignment). Although, Qvist et al. do not expressly teach the function recited in the claim, the claimed invention is anticipated as the structure is disclosed and the function is an inherent property. Therefore, the limitations of the claims are met by this reference.

14. Claims 1 and 68-69 are rejected under 35 U.S.C. 102(b) as being anticipated by Shriners Hospitals for Crippled Children (WO94/14070, 1994), cited on IDS filed April 30, 2004..

Shriners Hospitals for Crippled Children teach a sequence that is 100% identical to the peptide sequence set forth in SEQ ID NO: 3 of the instant application (see the alignment). Shriners Hospitals for Crippled Children also teach a method of measuring collagen (i.e., type I-III) degradation and ways to alter same. Therefore, the limitations of the claims are met by this reference.

Conclusion

15. No claims are allowable.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Hope A. Robinson whose telephone number is 571-272-0957. The examiner can normally be reached on Monday-Friday.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Kathleen Kerr, can be reached at (571) 272-0931. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Hope Robinson, MS

Patent Examiner 12/5/05

HOPE ROBINSON
PATENT EXAMINER

XX
SQ Sequence 1418 AA;

Query Match 100.0%; Score 132; DB 2; Length 1418;
Best Local Similarity 100.0%; Pred. No. 3.5e-07;
Matches 23; Conservative 0; Mismatches 0; Indels 0; Gaps 0;

Qy 1 ERGPPGPQGARGFPGTPGLPGVK 23
||||||||||||||||||||||||
Db 196 ERGPPGPQGARGFPGTPGLPGVK 218

RESULT 13
AAR71703
ID AAR71703 standard; protein; 1418 AA.
XX
AC AAR71703;
XX
DT 25-MAR-2003 (revised)
DT 17-OCT-1995 (first entry)
XX
DE Collagen alpha 1 (II) chain precursor.
XX
KW Collagen; antibody; immunoassay; metabolism; diagnosis; monitoring;
KW disorder; osteoporosis; metastatic progression; Paget's disease;
KW hyperthyroidism; bone; resorption; rheumatoid arthritis; osteoarthritis;
KW vasculitis syndrome.
XX
OS Homo sapiens.
XX
PN WO9508115-A1.
XX
PD 23-MAR-1995.
XX
PF 19-SEP-1994; 94WO-DK000348.
XX
PR 17-SEP-1993; 93DK-00001040.
XX
PA (OSTE-) OSTEOMETER AS.
XX
PI Qvist P, Bonde M;
XX
DR WPI; 1995-131456/17.
XX
PT Assaying collagen fragments in body fluid by immunoassay - using
PT antibodies raised against synthetic peptide(s) contg. potential
PT crosslinking sites, to diagnose and monitor disorders of collagen
PT metabolism, e.g. osteoporosis.
XX
PS Disclosure (Appendix A); Page 53; 87pp; English.
XX
CC Determination of collagen fragments in body fluids can be achieved by
CC immunoassay using antibodies directed against synthetic peptides derived
CC from collagen which contain sites of potential crosslinking. The method
CC is used to diagnose and monitor treatment of disorders of collagen
CC metabolism (degredation of type I collagen may indicate osteoporosis,
CC metastatic progression, Paget's disease, hyperthyroidism or other
CC conditions involving excessive bone resorption; degredation of type II
CC collagen may indicate rheumatoid arthritis or osteoarthritis; and of type
CC III collagen, vaculitis syndrome). The method can also be used to assess
CC the toxicity of a compound and to test drugs for their effect on collagen
CC metabolism. (Updated on 25-MAR-2003 to correct PN field.)
XX
SQ Sequence 1418 AA;

Query Match 100.0%; Score 132; DB 2; Length 1418;
Best Local Similarity 100.0%; Pred. No. 3.5e-07;
Matches 23; Conservative 0; Mismatches 0; Indels 0; Gaps 0;

Qy 1 ERGPPGPQGARGFPGTPGLPGVK 23
||||||||||||||||||||||||
Db 196 ERGPPGPQGARGFPGTPGLPGVK 218

RESULT 14
AAY96124
ID AAY96124 standard; peptide; 1418 AA.
XX
AC AAY96124;
XX
DT 19-DEC-2000 (first entry)
XX
DE Collagen type II alpha-1.
XX
KW Collagen type II; rheumatoid arthritis; osteoarthritis; assay; diagnosis.
XX
OS Homo sapiens.
XX
PN US6110689-A.
XX
PD 29-AUG-2000.
XX
PF 04-NOV-1997; 97US-00963825.
XX
PR 21-JAN-1994; 94US-00187319.
XX
PA (OSTE-) OSTEOMETER AS.
XX
PI Bonde M, Qvist P;
XX
DR WPI; 2000-586349/55.
XX
PT Assaying type I collagen fragments for diagnosing osteoporosis in
PT postmenopausal woman, involves contacting body fluid with synthetic
PT collagen peptide and antibody and quantifying by competitive binding
PT assay.
XX
PS Disclosure; Col 37-46; 41pp; English.
XX
CC The present sequence is that of human type II collagen alpha-1. The
CC invention is based on the discovery of the presence of particular
CC collagen fragments in body fluids of patients compared with those of
CC healthy subjects. These fragments are generated upon collagen degradation
CC and are partly characterised by the presence of potential sites for
CC crosslinking. A method for assaying collagen fragments in a body fluid
CC sample is based on the competitive binding to immunological binding
CC partners of collagen fragments in the sample and of synthetic peptides
CC derived from collagen and containing crosslinkable sites (see AAY96112-
CC 17). When considering the degradation of type II collagen, the assay can
CC be used as a means of identifying the presence of rheumatoid arthritis
CC and osteoarthritis
XX
SQ Sequence 1418 AA;

Query Match 100.0%; Score 132; DB 3; Length 1418;
Best Local Similarity 100.0%; Pred. No. 3.5e-07;
Matches 23; Conservative 0; Mismatches 0; Indels 0; Gaps 0;

Qy 1 ERGPPGPQGARGFPGTPGLPGVK 23
||||||||||||||||||||||||
Db 196 ERGPPGPQGARGFPGTPGLPGVK 218

RESULT 15
AAB35624
ID AAB35624 standard; protein; 1418 AA.
XX
AC AAB35624;
XX
DT 14-FEB-2001 (first entry)
XX
DE Human type II collagen.
XX
KW Type II collagen; arthritis; joint; ds.
XX
OS Homo sapiens.

Application No.: 10/674065

NOTICE TO COMPLY WITH REQUIREMENTS FOR PATENT APPLICATIONS CONTAINING NUCLEOTIDE SEQUENCE AND/OR AMINO ACID SEQUENCE DISCLOSURES

Applicant must file the items indicated below within the time period set the Office action to which the Notice is attached to avoid abandonment under 35 U.S.C. § 133 (extensions of time may be obtained under the provisions of 37 CFR 1.136(a)).

The nucleotide and/or amino acid sequence disclosure contained in this application does not comply with the requirements for such a disclosure as set forth in 37 C.F.R. 1.821 - 1.825 for the following reason(s):

[x] 1. This application clearly fails to comply with the requirements of 37 C.F.R. 1.821-1.825. Applicant's attention is directed to the final rulemaking notice published at 55 FR 18230 (May 1, 1990), and 1114 OG 29 (May 15, 1990). If the effective filing date is on or after July 1, 1998, see the final rulemaking notice published at 63 FR 29620 (June 1, 1998) and 1211 OG 82 (June 23, 1998).

[ ] 2. This application does not contain, as a separate part of the disclosure on paper copy, a "Sequence Listing" as required by 37 C.F.R. 1.821(c).

[ ] 3. A copy of the "Sequence Listing" in computer readable form has not been submitted as required by 37 C.F.R. 1.821(e).

[x] 4. A copy of the "Sequence Listing" in computer readable form has been submitted. However, the content of the computer readable form does not comply with the requirements of 37 C.F.R. 1.822 and/or 1.823, as indicated on the attached copy of the marked -up "Raw Sequence Listing."

[ ] 5. The computer readable form that has been filed with this application has been found to be damaged and/or unreadable as indicated on the attached CRF Diskette Problem Report. A Substitute computer readable form must be submitted as required by 37 C.F.R. 1.825(d).

[ ] 6. The paper copy of the "Sequence Listing" is not the same as the computer readable form of the "Sequence Listing" as required by 37 C.F.R. 1.821(e).

[ ] 7. Other:

8. Applicant Must Provide:

[x] An initial or substitute computer readable form (CRF) copy of the "Sequence Listing".

[x] An initial or substitute paper copy of the "Sequence Listing", as well as an amendment directing its entry into the specification.

[x] A statement that the content of the paper and computer readable copies are the same and, where applicable, include no new matter, as required by 37 C.F.R. 1.821(e) or 1.821(f) or 1.821(g).

For questions regarding compliance to these requirements, please contact:

- For Rules Interpretation, call (703) 308-4216 or (703) 308-2923
- For CRF Submission Help, call (703) 308-4212
- For PatentIn software Program Support:
  - HELP DESK: (703) 739-8559, ext 508, M-F, 8 AM to 5 PM EST except holidays
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